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PHILIP S. JOHNSON
JOHNSON & JOHNSON
ONE JOHNSON & JOHNSON PLAZA
NEW BRUNSWICK, NJ 08933-7003

EXAMINER	
QAZI, SABIHA NAIM	
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BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Application Number: 10/022,138
Filing Date: December 13, 2001
Appellant(s): SCHULTZ ET AL.

Joseph S. Kentofflo
For Appellant

EXAMINER'S ANSWER

This is in response to the appeal brief filed 3/16/2009 appealing from the Office action mailed on 8/21/2008.

(1) Real Party in Interest

A statement identifying by name the real party in interest is contained in the brief.

(2) Related Appeals and Interferences

The examiner is not aware of any related appeals, interferences, or judicial proceedings which will directly affect or be directly affected by or have a bearing on the Board's decision in the pending appeal.

(3) Status of Claims

The statement of the status of claims contained in the brief is correct.

(4) Status of Amendments after Final

The appellant's statement of the status of amendments after final rejection contained in the brief is correct.

(5) Summary of Claimed Subject Matter

The summary of claimed subject matter contained in the brief is correct.

(6) Grounds of Rejection to be reviewed on Appeal

The appellant's statement of the grounds of rejection to be reviewed on appeal is correct.

(7) Claims Appendix

The copy of the appealed claims contained in the Appendix to the brief is correct.

(8) Evidence Relied Upon

US 5,858,405	GAST	1-1999
EP 0503,521	de HAAN, Pieter	09-1992

Morita, Masami et al. "Physiochemical Properties of Crystalline Lactose. II, Effect of crystallinity on mechanical and structural properties", Chem. Pharm. Bull. Vol. 32 (1984)., pp. 4076-4083.

Jain, R. et al "Stability of a hydrophobic drug in presence of hydrous and anhydrous lactose" European Journal of Pharmaceutics and Biopharmaceutics, Vol. 46 (1998), pp. 177-182.

Buckton, G. et al. "The influence of additives on the recrystallisation of amorphous spray dried lactose", International Journal of Pharmaceutics, No. 121 (1995), pp.81-87.

Budavari, S., Editor, Merck Index, 12th edition, (1996), page 632 (3751).

Sebhatu, T. et al., "Assessment of the degree of disorder in crystalline solids by isothermal microcalorimetry", International Journal of Pharmaceutics, 104 (1994), 135-144.

(9) Grounds of Rejection

The following ground(s) of rejection are applicable to the appealed claims:

First Rejection

Claims 1, 6 and 7 are rejected under 35 U.S.C. 103(a) over GAST in view of MORITA, MERCK; JAIN et al; Sebhatu et al, Rialker et al and BOUCKTON et al.

GAST teaches a hormonal product with an excipient in crystalline and non-crystalline form, which embraces Appellant's claimed invention. See the entire documents especially examples 1 and 2, claims, lines 11-19 and lines 31-67 in col. 7 of GAST.

MORITA teaches that lactose has been widely used for solid pharmaceutical preparations and many grades are available for example official grade, crystalline, anhydrous, spray dried, or granulated lactose. Anhydrous and spray-dried and granulated lactose preparations have been used in direct compression applications. This classification is based on the manufacturing methods. On the other hand lactose has four crystallographic forms, namely alpha-monohydrate, alpha-anhydrate, beta-anhydrate and amorphous form. See the entire document especially abstract, Tables I-III and page 4076 of the reference.

MERCK in section 3751 teaches that estrone *can be* crystallized.

JAIN teaches the stability of a hydrophobic drug in presence of hydrous and anhydrous lactose. See the entire document especially abstract and introduction.

SEBHATU et al., Rialkar et al., BOUCKTON et al. and JAIN et al. teach the use of lactose. See the entire documents.

Instant claims differ from GAST in claiming a broader scope of non-crystalline steroid hormone. The difference between the instant invention and GAST is that the instant invention specifically claims the non-crystalline form while GAST is silent on specifically naming

crystallization (Even though GAST discloses "Preferred salts of estrone include but are not limited to the sodium and piperate salt," it does not specifically use the words *crystalline* or *non-crystalline*) and MORITA et al which teaches the use of lactose in pharmaceutical preparations. MERCK in cited section 3751, teaches that estrone *can be* crystallized which means that it was ***not*** crystalline before. Also it can be used as estrones or its salts which can be crystallized or non-crystallized. GAST teaches the use of **lactose** in the formulation see example 1 on page 13 (example 1).

It would have been obvious to one skilled in the art to prepare beneficial compositions for hormone replace therapy and other estrogen deficiencies because GAST teaches the limitations of the instantly claimed invention. Since GAST is silent on crystallization and lactose, the Examiner has cited MORITA and BOUCKTON which teach use of lactose in pharmaceutical preparations and Budavari (MERCK), which teaches the crystallization process of estrone to show that estrone exists in both non-crystalline and crystalline forms. Likewise, SEBHATU et al., RIALKAR et al. and JAIN all teach the stability of hydrophobic drugs in presence of hydrous and anhydrous lactose, providing further objective evidence suggesting the use of lactose.

Second Rejection

Claims 1, 6 and 7 are rejected under 35 U.S.C. 103(a) over de HAAN, PETER (EP 0503,521 A1) and Budavari (MERCK). Both the reference teaches the formation of a tablet containing steroid specially progesterone and estrogen and excipient lactose which embraces Appellant's claimed invention.

HAAN teaches dry pharmaceutical preparations containing ultra-low doses of one or more micronized steroidal medicinal agents in combination with a primary excipient having a high binding affinity and low demixing potential for the steroidal medicinal agent. Such excipient include spray-dried polyalcohols, granulated a-lactose monohydrate (**essentially 100 % latose**), and mixture thereof. A steroidal medicinal agent is one having a chemical structure containing a **cyclopentanoperhydrophenanthrene** backbone. The reference further teaches the formation of a tablet containing steroid specially **progesterone** and estrogen and more particularly progestetogens include 3-ketodesogesterel, (etonogestrel), desogestral, levo-norgestrel, norgerstrel, gestodene, and other compounds with similar progestogenic activity. See the entire document especially abstract, lines 16-50, page 3; lines 27-59, page 4; lines 48-58, page 5; lines 1-19, page 6; examples and claims..

MERCK in section 3751 teaches that estrone *can be* crystallized.

It would have been obvious to one skilled in the art at the time the invention was filed to prepare beneficial compositions as oral steroid hormone product comprising norgestimate in admixture with lactose because the reference teach the advantages of the use of lactose with a steroidal medicinal agent is one having a chemical structure containing a **cyclopentanoperhydrophenanthrene** backbone. The reference further teaches the formation of a tablet containing steroid specially **progesterone.** Norgestimate is progesterone. The motivation has been provided by the prior art to prepare such a composition. Further the term comprising in present claims allows other ingredients may be added.

(10) Response to Argument

First Rejection

Examiner disagrees with the arguments because Appellants are addressing every reference separately and the rejections are based on the combined teachings of the cited references. It has been decided by the courts that "One cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references." See *In re Keller*, 642 F.2d 413, 208 SPQ 871 (CCPA 1981); *In re Merck* & Co., Inc., 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). See MPEP 2145. In the present case rejections are made in combination of references.

Appellant argue that "there is no teaching or suggestion in GAST of such a product wherein the steroid hormone is in non crystalline form. Appellant further argue that MORITA relates only to lactose excipient which includes non-crystalline form and does not says about hormonal products. JAIN merely states that a hydrophobic drug may be stabilized in presence of hydrous and anhydrous lactose. SEBHATU and BUCKTON relate to the use of lactose in pharmaceutical preparations".

Examiner believes that it would have been obvious to one skilled in the art to prepare an oral steroid hormone product comprising norgestimate and lactose in non-crystalline form as has been claimed, (the references teach the formulation of estrogen/progestins combinations together with lactose) because (1) GAST teaches "norgestimate" which is claimed progestin (see lines 13-17 and 20-27 in column 3). It teaches oral contraceptives containing estrogen and progestin and the formulation of hormonal product with lactose (examples 1 and 2 in column 2). The progestins norgestimate, desogestrel (which are included in Appellants claim or specification),

and their formulations with lactose have been taught by GAST (2) MORITA teaches that lactose has been widely used for solid pharmaceutical preparations and are available in crystalline, anhydrous, spray dried, or granulated lactose. (3) MERCK teaches the crystallization process of estrone which shows that estrone which is a steroid, exists in both non-crystalline and crystalline forms, (4) JAIN teaches the stability of a hydrophobic drug in presence of hydrous and anhydrous lactose (5) BUCKTON teaches the influence of additives on the amorphous spray dried lactose and (6) SEBHATU teaches that spray dried lactose for direct compression are semi-crystalline, with regions of amorphous contents within their structure.

No criticality of invention was noted in claims. Claims contain no additional conditions of dissolution as has been described in lines 16-25 on page 10 as argued. Similarly, it does not contain the stability of amorphous norgestimate as presented in Table 6 which has been argued. The specification discloses in Table 1 page 10 two dissolution rates at 5 mins. and 60 mins. At 5 mins there is no difference between amorphous and crystalline norgestimate and at 60 mins. The specification discloses that "As anticipated, lactose recrystallized between 0-2 days. Initiation of norgestimate recrystallization was noted between 17-22 days. Norgestimate remained partially crystalline for at least 44 days (Table 2, page 14).

Second Rejection

Appellant argues that EP '521 does not teach the claimed invention. Examiner disagrees because EP '521 teaches low dose dry composition pharmaceutical preparations containing potent steroidal medicinal agents which includes progestins as claimed. The reference teaches

that steroidal medicinal agent is one having a chemical structure containing a **cyclopentanoperhydrophenanthrene backbone**.

This backbone is present in progestins norgestimate (claimed), **3-ketodesogesterel,** (etonogestrel), **desogestrel** (disclosed in the Appellants specification), levo-norgestrel, norgerstrel and gestodene. The reference further teaches the formation of a tablet containing steroid specially **progesterone** and estrogen and more particularly progestetogens include **3-ketodesogesterel,** (etonogestrel), **desogestral,** levo-norgestrel, norgerstrel, gestodene, and other compounds with similar progestogenic activity. Example 1 of the reference on page 6 contains desogestrel and 3-ketodesogestrol (example VIII on page 9) which is listed in appellant's specification. Different type of **lactose** has been taught in example II and VI which includes alpha lactose and spray-dried lactose. The drug may be present in crystalline or non crystalline forms.

Appellants argue that there is no direct teaching by MERCK that steroid estrone can be crystalline form. Appellant further argue that "the reference still fails to teach the steroidal hormonal product that includes the steroid hormone norgestimate". Examiner disagrees because MERCK teaches that estrone can be in crystalline form meaning that main form that exists is non-crystalline.

Examiner again disagrees with the arguments because it has been decided by the courts that "One cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references." In re Keller, 642 F.2d 413, 208 SPQ 871 (CCPA 1981); In re Merck & Co., Inc., 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). See MPEP 2145.

(11) Related Proceeding(s) Appendix

No decision rendered by a court or the Board is identified by the examiner in the Related Appeals and Interferences section of this examiner's answer.

For the above reasons, it is believed that the rejections should be sustained.

Respectfully submitted,

/Sabiha Qazi/

Primary Examiner, Art Unit 1612

Conferees:

/Frederick Krass/

Supervisory Patent Examiner, Art Unit 1612

/Ardin Marschel/

Supervisory Patent Examiner, Art Unit 1614